REMARKS

I. Amendment to the Specification. As requested by the Examiner, the specification on page 1 has been amended to reflect the status of prior application no. 09/270,910. No new matter is added by this amendment.

II. Status of the Claims. Claims 36-96 are pending. Claims 44-65 and 74-96 have been withdrawn from consideration by the Examiner as being directed to non-elected subject matter.

Claims 36 and 66 have been amended to be directed respectively to a *Bet v 1* allergen from the order *Fagales* and a mutant allergen derived from a naturally-occurring allergen within the order *Fagales* that is homologous to *Bet v 1*. Support for the amendments is found in the specification at, e.g., page 15, lines 29-33 and page 24, lines 8-14. Claim 66 has also been amended to delete non-elected subject matter.

By this Amendment, no new matter has been added to the application.

III. Examiner's Interview. On July 30, 2007, Applicants' representative Mitchell Bernstein conducted a personal interview at the USPTO with Examiners Rooney, Haddad, Szperka, Ewoldt and SPE Chan, at which time the pending rejections were discussed. Applicants' representative thanks the Examiners for the courtesies extended during the interview. No agreement on the claims was reached.

IV. Double Patenting. Claims 36-43 and 66-73 have been provisionally rejected for obviousness-type double patenting over claims 1-22, 25, 26, 28, 35, 37-39, 64 and 66-85 of co-pending application no. 10/001,245 ("the '245 application"). The '245 application has not issued as a patent. Accordingly, it is requested that the instant rejection be held in abeyance.

V. Priority Statement. The Examiner has requested that the common assignee of the instant application and the co-pending '245 application state which entity is the prior inventor of the alleged conflicting subject matter in claims 36-43 and 66-73 of the instant application and claims 1-22, 25, 26, 28, 35, 37-39, 64 and 66-85 of the '245 application. In response, in order for the instant response to be complete, and without conceding that that there is conflicting subject matter claimed in the '245 and '553 applications (which Applicants do not believe to be the case),

the common assignee of the '245 application and the instant application indicates that the subject matter claimed in the instant '553 application is the prior invention.

VI. Response to Rejections. The rejections set forth in the Office Action are addressed as follows.

(i) Rejections Under 35 U.S.C. § 112, first paragraph (written description). Claims 36, 38-43 and 66-73 are rejected for alleged lack of written description. The Examiner's position is that "[o]ther than the specific recombinant allergens recited in claim 37, there is inadequate written description of the structure and functions for any other recombinant allergen as set forth in claims 36, 38-43 and 66-73." The rejection is traversed on the grounds that the specification provides sufficient relevant identifying characteristics coupled with sufficient examples to demonstrate that that the inventors were in possession of the claimed invention at the time the application was filed.

The specification provides adequate written description for claims 36, 38-43 and 66-73. The written description requirement requires that the specification provide disclosure that allows one of ordinary skill in the art of the invention to "recognize that [the inventor] invented what is claimed." *Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572 (Fed. Cir. 1997); *see also Vas-Cath Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64 (Fed. Cir. 1991) (Applicant "must convey with reasonable clarity to those skilled in the art that ... he or she was in possession *of the invention.*") (emphasis in original). The written description requirement "ensure[s] that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as detailed in the patent specification." *Reiffin v. Microsoft Corp.,* 214 F.3d 1342, 1354 (Fed. Cir. 2000). The written description requirement is met by providing sufficient structural, physical and/or functional properties that describe a genus and/or a sufficient members of genus that show the inventors were in possession of the claimed invention. *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3d 1559, 1567-68 (Fed. Cir. 1997). Functional language may provide adequate written description "if in the knowledge of the art the disclosed function is sufficiently correlated with a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.,* 314 F.3d 1313, 1332 (Fed. Cir. 2003) *citing Enzo Biochem, Inc. v. Gen-Probe, Inc.,* 296 F.3d 1316, 1324 (Fed. Cir. 2002).

The instant application sets forth the invention of claims 36, 38-43 and 66-73 in sufficient detail to show that Applicants were in possession of the claimed invention. The claims are drawn to recombinant *Bet v 1* allergens from the order *Fagales* (*see* claim 36) and mutant allergens derived from naturally-occurring allergens within the order *Fagales* that are homologous to *Bet v 1* (*see* claim 66) having a substitution of a solvent-accessible amino acid residue that is conserved among *Bet v 1* allergens from the order *Fagales* in a B-cell epitope of the allergen, and which has reduced IgE binding compared to the naturally-occurring *Bet v 1* allergen from which it is derived and which has an α-carbon backbone tertiary structure that is preserved compared to the α-carbon backbone tertiary structure of the naturally occurring allergen.

The specification provides adequate written description sufficient to show that the inventors had possession of any such mutant *Bet v 1* allergens from the order *Fagales* or mutant allergens derived from a naturally-occurring allergen within the order *Fagales* that is homologous to *Bet v 1*. Hence, the specification discloses the existence of dominant IgE binding epitopes that are proposed to be constituted by tertiary structure dependent coherent surface areas large enough to accommodate antibody binding, and which are conserved among homologous allergens from related species. Specification at page 13, lines 11-18. The specification discloses that the amino acids to be mutated are found in a patch of conserved amino acid residues being coherently connected over at least 400 $Å^2$ on the surface of the three dimensional surface of the allergen as defined by having a solvent accessibility of at least 20%. Specification at, e.g., page 20, lines 9-20. The specification further sets cut that homology among homologous proteins within a taxonomical order may be used to identify amino acids for substitution. Specification at page 35, lines 6-34. Further criteria to identify preferred amino acids for substitution are set forth on pages 20, line 31 through page 21, line 2 (preferentially select amino acids among most water soluble, near center of conserved patch and substitute polar amino acid with another polar amino acid and non-polar amino acid with another non-polar amino acid.) Thus, the specification describes the structural features of the amino acid substitution that are to be substituted on any allergen.

The specification further gives additional details on the structural features of *Bet v 1* and related proteins that further show possession of the invention of claims 36-43 and 66-73. Thus, at the time the application was filed, the structural basis for allergic *Bet v 1* cross reactivity had been

reported to be associated with three patches on the molecular surface of *Bet v 1*. Specification at page 24, line 34 through page 25, line 2. Amino acids within these patches that may be substituted were identified by aligning 122 sequences homologous to SEQ ID NO: 37, of which 57 sequences originated from taxonomically related species. Specification at page 26, lines 1-14. The specification at page 29, line 5-12 further identifies amino acid substitutions in *Bet v 1* (SEQ ID NO: 37) (Thr10Pro, Asp25Gly, Asn28Thr, Lys32Gln, Glu45Ser, Asn47Ser, Lys55Asn, Thr77Ala, Pro108Gly) that may be used to make recombinant mutant allergens with single mutations or multiple mutations (Asn28Thr + Lys32Gln and "triple patch" mutant Glu45Ser, Asn28Thr + Lys32Gln, Pro108Gly). Thus, the specification gives particular structural features and examples that demonstrate possession of any recombinant *Bet v 1* allergen, as called for in the claims.

Moreover, as disclosed in the specification, proteins within the order *Fagales* that are homologous to SEQ ID NO: 37 are highly conserved in sequence and structure. The features used to identify amino acid substitutions to be made in *Bet v 1* of SEQ ID NO: 37 are thus also sufficient to show possession of mutant allergens of any *Bet v 1* homologous protein within the order *Fagales*. Related allergens are cross-reactive, allergic patients often react to several closely related species, and homologous allergens inhibit binding of IgE to each other. Specification at page 13, lines 18-36. Thus, the structural features that define an IgE epitope are conserved among *Bet v 1* homologous proteins. Moreover, *Bet v 1* of SEQ ID NO: 37 shows about 90% amino acid identity with major allergens from pollens within the *Fagales* order and birch pollen allergic patients often show clinical symptoms of allergic cross-reactivity with *Bet v 1* homologous proteins from *Fagales* species. Specification at page 24, lines 8-14.

In setting forth the instant rejection, the Examiner cites *Eli Lilly*, *supra*. The nature of the instant invention and the disclosure of the instant specification, however, are very different from *Eli Lilly*. In *Eli Lilly*, the Federal Circuit held that the disclosure of the sequence of a rat insulin cDNA did not provide adequate written description for the insulin cDNA sequence of every vertebrate. *Eli Lilly* at 1566-67. In *Eli Lilly*, however, the specification failed to provide any features that described the claimed vertebrate insulin cDNA. The Court found that the claimed cDNA were described solely by their function or how to obtain them. The instant case is inapposite to *Eli Lilly*. In Eli Lilly the claims were directed to unknown cDNA sequences. The instant claims,

by contrast, are drawn to mutant allergens that are derived by making substitutions in a family of allergens, i.e., *Bet v 1* homologous proteins from the order *Fagales*, with closely related sequences. In *Eli Lilly*, no structural features were provided that correlated with the function of the claimed vertebrate insulin cDNA. In the instant case, the specification provides that substituted amino acids are those amino acids that are conserved, solvent accessible amino acids that are part of IgE epitopes and that, in turn, IgE epitopes of *Bet v 1* homologous proteins are found within three patches on the surface of *Bet v 1* proteins. Accordingly, the written description requirement is satisfied in the instant case because the "in the knowledge of the art the disclosed function [i.e., IgE binding] is sufficiently correlated to a particular, known structure [i.e., conserved, solvent accessible amino acids present in coherently connected patches on the surface of *Bet v 1* homologous allergens]." *See Amgen, Inc.* at 1332, *discussing Enzo Biochem, Inc.* at 1324.

Nor does the decision of the Board of Patent Appeals and Interferences in *ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)) support a finding that the instant specification fails to provide adequate written description for the pending claims. In *Kubin*, the Board upheld the rejection of a claim directed to isolated polynucleotides encoding polypeptides that (1) "are at least 80% identical to amino acids 22-221 of SEQ ID NO: 2" (i.e., the amino acid sequence for the extracellular domain of the protein natural killer cell activation inducing ligand ("NAIL") lacking the NAIL signal sequence) and (2) which bind to the glycoprotein CD 48. *Id.* at 1417. The specification in *Kubin* disclosed the sequence of two nucleic acids within the scope of the claim and three fusion proteins whose nucleic acid sequences would fall within the scope of the claim. *Id.* None of these sequences varied amino acids 22-221 of SEQ ID NO: 2. *Id.*

The Board in *Kubin* found that the Applicant had failed to describe what domains of within amino acids 22-221 of SEQ ID NO: 2 correlated with the function of binding CD 48, and thus the Applicant had not described which NAIL amino acids could be varied and still maintain CD 48 binding. *Id.* Citing *Eli Lilly*, the Board found that in the absence of a structure-function correlation, the claim merely defined the invention by function, which was not sufficient to satisfy the written description requirement.

Kubin is distinguished from the instant case for much the same reasons as *Eli Lilly*. In *Kubin*, the Applicant failed to provide any features of amino acids 22-221 of SEQ ID NO: 2 that

correlated with binding to CD 48. As set forth above, the instant specification, in contrast, sets forth structural features that allow one of ordinary skill in the art to identify amino acids in *Bet v 1* homologous proteins that contribute to IgE binding and thus may be mutated to obtain mutant allergens with reduced IgE binding. Furthermore, whereas in *Kubin* the Applicant failed to disclose any polynucleotides encoding NAIL protein that varied in amino acids 22-221, the instant applications identifies amino acid substitutions in *Bet v 1* (SEQ ID NO: 37) (Thr10Pro, Asp25Gly, Asn28Thr, Lys32Gln, Glu45Ser, Asn47Ser, Lys55Asn, Thr77Ala, Pro108Gly) that may be used to make recombinant mutant allergens with single mutations or multiple mutations (Asn28Thr + Lys32Gln and "triple patch" mutant Glu45Ser, Asn28Thr + Lys32Gln, Pro108Gly) in which a conserved, solvent accessible amino acid in *Bet v 1* is substituted such that the mutant recombinant allergen derived thereby exhibits reduced IgE binding and retains the native α-carbon backbone structure of *Bet v 1*. Moreover, each of the mutants tested (Glu45Ser; Pro108Gly; Asn28Thr + Lys32Gln; Glu45Ser, Asn28Thr + Lys32Gln, Pro108Gly) had the properties called for in the instant claims. Thus, the instant application provides working examples for recombinant *Bet v 1* allergens with mutations in conserved, solvent accessible amino acids in patches on the surface of *Bet v 1* with reduced IgE binding and which retain a native α-carbon backbone structure, whereas the Applicant in *Kubin* failed to provide any working examples of polynucleotides encoding a polypeptide at least 80% identical to amino acids 22-221 of SEQ ID NO: 2 and which bind CD 48.

In short, as with *Eli Lilly*, the Applicant in *Kubin* failed to provide any structural features that correlated with the function of the polypeptide called for in the claim, whereas the instant specification sets out the features of *Bet v 1* homologous proteins that correlate with the function of IgE binding that is called for in the claim and which allow one of ordinary skill in the mutant art to make recombinant allergens with reduced IgE binding but which retain a native backbone structure. Thus, the basis of the Board's decision in *Kubin* does not apply to the instant claims.

For at least all of the reasons set forth above, the specification provides adequate written description for the full breadth of the instantly claimed invention. Reconsideration of claims 36, 38-43 and 66-73 withdrawal of the rejection thereof for lack of written description is requested.

(ii) Rejections Under 35 U.S.C. § 112, first paragraph (enablement). Claims 36, 38-43 and 66-73 are rejected for alleged lack of enablement. The claims are drawn to recombinant *Bet v 1* allergens from the order *Fagales* (*see* claim 36) and mutant allergens derived from a naturally-occurring allergen within the order *Fagales* that is homologous to *Bet v 1* (*see* claim 66) having a substitution of a solvent accessible amino acid residue that is conserved among *Bet v 1* allergens from the order *Fagales* in a B-cell epitope of the allergen, and which has reduced IgE binding compared to the naturally-occurring *Bet v 1* allergen from which it is derived and which has an α-carbon backbone tertiary structure that is preserved compared to the α-carbon backbone tertiary structure of the naturally occurring allergen.

The specification enables the full scope of these claims. Each of the steps required to make and use the claimed invention can be carried out using the procedures set forth in the instant specification and routine procedures that were well known to those of ordinary skill in the art as of the filing date of the application. Hence, as of the filing date of the application, it was routine to identify homologous allergens, including homologous *Bet v 1* allergens from the taxonomic order *Fagales* and identify conserved amino acids in the homologous allergens using commercially available alignment programs. The specification at pages 26, lines 1-14 sets forth a method for using BLAST to identify sequences homologous to *Bet v 1* of SEQ ID NOS: 36-37 in GenBank and EMBL databases and align these homologous sequences with the CLUSTAL W program. This procedure identified 122 sequences homologous to *Bet v 1* having the sequence of SEQ ID NO: 37, of which 57 sequences originated from taxonomically related species. Specification at page 26, lines 12-15. Accordingly, the application sets forth explicit methods to identify conserved amino acids for *any Bet v 1* homologous allergen within the taxonomic order *Fagales*.

Using information and techniques set forth in the application and other techniques routine at the time the application was filed, one of ordinary skill in the art would have further been able to determine which of the conserved amino acids identified using the methods described above is a surface-exposed amino acid residue of a B cell epitope of any *Bet v 1* homolog. Hence, by the time the application was filed, the crystal structure of *Bet v 1* protein had been determined and published. *See reference to* Ghajhede et al., 1996, *Nature Structural Biol.* 3:1040-1045 at page 24, line 35 of the specification. Knowledge of the crystal structure allows identification of solvent accessible amino acids. Furthermore, *Bet v 1* homologous proteins from the order *Fagales* are about 90% identical. Specification at page 24, lines 8-14. This high level of identity means that using the

knowledge of the crystal structure of a *Bet v 1* protein of SEQ ID NO: 37 to identify solvent accessible amino acids and the alignment procedures discussed *supra* allows identification of the solvent accessible amino acids of *any Fagales* allergen homologous to *Bet v 1*. Accordingly, using procedures set forth in the application, at the time the invention was filed, one of ordinary skill in the art would have been able to identify solvent accessible amino acids on any *Fagales* allergen homologous to *Bet v 1*.

Furthermore, the criteria for choosing which amino acids of *Bet v 1* homologues are present in B-cell epitopes and that are to be substituted are set forth in the specification, e.g., at pages 14-15. Using the methods discussed *supra* the amino acid were identified as being conserved with more than 70% identity in *Bet v 1* homologous proteins within the taxonomic order *Fagales* (specification at page 14-15, bridging paragraph) and as being present in a patch of conserved amino acid residues coherently connected over at least 400 $Å^2$ of the surface of the three-dimensional surface of the allergen having a solvent accessibility of at least 20% (specification at page 15, lines 6-11). At the time the application was filed, three such patches were known for *Bet v 1* of SEQ ID NO: 37 that could be identified to be common to the known major tree pollen allergens. Specification at pages 24-25, bridging paragraph. Thus, the methods set out in the specification can used to identify B-cell epitopes on the surface of *any Bet v 1* homologous allergen from the taxonomic order *Fagales*. The specification further specifies that the mutant amino acid substitution should be the substitution of an amino residue in at least one patch with an amino acid that is not conserved at the position of the substitution, while preserving the tertiary structure of the allergen molecule. Specification at page 15, lines 13-14.

Finally, using the guidance contained in the specification, as of the filing date of the application, one of ordinary skill in the art would have been able to determine which amino acid substitutions can be made while preserving the α-carbon backbone tertiary structure of the naturally occurring *Bet v 1* homologous allergen while reducing specific IgE binding. Hence, the specification sets forth at page 18, lines 8-16 that crystallography, NMR or CD-spectra (all routine techniques) can used to determine conservation of an α-carbon backbone in a recombinant allergen. These techniques could have been used to determine conservation of the α-carbon backbone of *any Bet v 1* homologous protein from the order *Fagales*. Lastly, the specification sets forth that IgE

binding can be determined using a fluid-phase IgE-inhibition assay using the pool of serum IgE derived from allergic patients (see, e.g., page 33, lines 5-8).

Accordingly, the specification gives extensive guidance that allows one of ordinary skill in the art to determine which conserved amino acids of any *Bet v 1* homologous allergen from the taxonomic order *Fagales* should be substituted, which type of substitution was to be made and which substitutions would have the claimed properties of retaining conserved tertiary structure and reduced IgE binding. On the date the application was filed, therefore, the specification gave clear guidance to one of ordinary skill in the art on how to make and use the presently claimed invention.

Furthermore, using the methods set forth within the four-corners of the specification and techniques well know at the time the application was filed, Applicants have provided working examples recombinant mutant *Bet v 1* allergens, as claimed.

Examination of the factors set forth in *In re Wands* (858 F2d 731, 8 USPQ2d 1400 (Fed Cir 1988)), leads to the conclusion that the full scope of the instant claims is enabled.

Breadth of the claims. The claims have been restricted to *Bet v 1* allergens originating from the taxonomic order *Fagales*. Such allergens are well known and highly studied among those of ordinary skill in the art. As discussed above, at the time the application was filed, the crystal structure of *Bet v 1* (SEQ ID NO: 37) was known and it was known that *Bet v 1* homologues from the order *Fagales* exhibit about 90% identity.

Nature of the invention. The nature of the invention is making substitutions in a known allergen protein that lowers the IgE binding of the allergen but retains the three dimensional structure of the allergen.

The level of ordinary skill in the art. The level of skill in the art is high. All of the methods needed to practice the claimed invention were in routine use at the time the application was filed.

The state of the prior art. The state of the art is such that it is known that *Bet v 1* allergens include dominant IgE epitopes that reside in patches the surface of *Bet v 1* homologous, that *Bet v 1* homologous proteins from the order *Fagales* share a high level of identity and exhibit cross reactivity.

The existence of working examples. The application provides working examples of two *Bet v 1* mutants with a single substitution, one *Bet v 1* mutant with a double substitution, and one *Bet v 1* "triple patch" mutant that includes four point mutations, one mutation in each in two of

the patches identified on the surface of *Bet v 1* and two mutations in the third patch identified on the surface of *Bet v 1*.

The level of predictability. Each of the working examples set forth above has the properties called for in the pending claims. Moreover, the specification includes the results for all of the mutants that had been made at the time the application was filed. Thus, it is apparent that claimed mutant allergens may be predictably derived using the methods set forth in the application.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure. The predictability with which *Bet v 1* mutant allergens having the properties called for in the claims were obtained indicates that little experimentation is required to make and use the claimed invention. Moreover, each of the steps required to practice the invention were well known and predictable at the time the invention was made, requiring no experimentation. With specific regard to identifying mutant allergens with native tertiary structure and reduced IgE binding, as discussed *supra*, using methods set forth in the specification, it would have been routine for one of ordinary skill in the art to identify *any* mutant allergen with these characteristics. Given the routine nature of the methods, the need to identify successful substitutions that retain tertiary structure of the original allergen and have reduced IgE binding from substitutions that do not have these characteristics is not sufficient to constitute undue experimentation. (*In re Wands*, *supra*, (screening negative hybridomas to find one that makes the desired antibody is not undue experimentation.))

Amount of direction or guidance. Applicants have discussed at length *supra* that the specification gives extensive guidance in identifying and aligning allergen homologues, selecting a surface-exposed amino acid for substitution and which type of substitution is to be made, determining which mutant allergens bearing a substitution retain the tertiary structure of the original allergen and which mutant allergens have reduced IgE binding, compared to the original allergen.

Certain issues raised by the Examiner are addressed as follows.

The Examiner states that the specification does not define a particular algorithm to be used to determine homology and that it is known that parameters such as gap length, substitution matrices and percent cutoffs influence homology calculations. In response, as already noted above, the specification at pages 26, lines 1-14 sets forth a method for using BLAST to identify sequences homologous to *Bet v 1* of SEQ ID NOS: 36-37 in GenBank and EMBL databases and align these homologous sequences with the CLUSTAL W program. This procedure identified 122 sequences

homologous to *Bet v 1* having the sequence of SEQ ID NO: 37, of which 57 sequences originated from taxonomically related species. Specification at page 26, lines 12-15. Accordingly, the application sets forth explicit methods to align protein sequences and identify conserved amino acids for *any Bet v 1* homologous allergen within the taxonomic order *Fagales*. Moreover, given the large number of *Bet v 1* homologous sequences, the alignment obtained would not be expected to vary with routine changes in the parameters identified by the Examiner. Thus, the specification provides all of the information required to identify conserved amino acids within *Bet v 1* homologous proteins within the order *Fagales*.

The Examiner raises objections based on the assertion that there is insufficient guidance and working examples as to which amino acid residues in the B cell epitope of any *Bet v 1* allergen can be substituted and still retain the α-carbon backbone structure and have reduced IgE binding as compared to the naturally occurring allergen. The Examiner's objection is not well taken. As set out above, the specification includes provides such guidance in setting out that such amino acid residues are conserved, solvent accessible amino acids in the three patches found on the surface of *Bet v 1* homologous proteins. Each of the *Bet v 1* mutant allergens made according to the methods set forth in the specification described and tested for IgE binding and tertiary structure exhibited reduced IgE binding and retained a native α-carbon backbone structure. Thus, the results set forth in the specification directly refute the Examiner's assertion that further information is needed to determine which amino acids in *Bet v 1* should be mutated to make and use the claimed invention. The high degree of homology among *Bet v 1* homologous proteins within the order *Fagales* further indicates that the results obtained for the *Bet v 1* examples will apply to any *Bet v 1* homologous protein within the order *Fagales*.

The Examiner cites Fig. 7 in the context of noting that various mutations in *Bet v 1* are not all necessarily predictive of IgE binding while the overall α-carbon backbone tertiary structure is preserved. In response, it is noted that Fig. 7 gives the results of an experiment designed to measure the IgE binding of the non-patch mutant *Bet v 1* Glu60Ser. *See* specification at page 37, lines 3-8 ("Glutamic acid in position 60 show[s] a high degree of solvent-exposure (60%) however, it is not located in a molecular surface patch common for *Fagales* allergens.") Thus, the results shown in Fig. 7 indicating that the Glu60Ser mutant did not show any significant effect on the IgE binding properties of *Bet v 1* are entirely consistent with the disclosure in the specification that

substitutions of amino acids within the surface patches of *Bet v 1* lower the IgE. Specification at page 37, line 31 through page 38, line 4. Accordingly, the results obtained with the non-patch mutant *Bet v 1* Glu60Ser are strong evidence that the specification provides sufficient detail to make and use the instant invention.

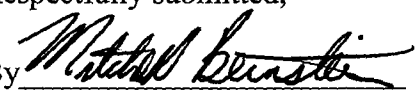
The Examiner cites Skolnick et al. and Attwood as indicating that it is difficult to predict structure or function from amino acid sequences. Applicants believe respectfully that the Examiner has misapplied these references to the instant claims. Skolnick et al. and Attwood are directed to general methods of predicting protein structure and function based on sequence. In citing the references, the Examiner has failed to distinguish predictive methods based on different levels of homology between proteins, the complexity of the functional unit to be predicted from the sequence and whether or not a the three dimensional structure is know for a protein family member. Accordingly, the Examiner's casual and generalized statements that Skolnick et al. and Attwood teach the unpredictability of predicting structure or function from sequence carry little weight when applied to the instant case, where the prediction of protein function is based on closely related homologous *Bet v 1* allergens wherein the tertiary structure has been determined for at least one *Bet v 1* homologue and wherein the function to be ascertained is IgE binding.

For the reasons set forth above, Applicants respectfully submit the rejection of the claims under 35 U.S.C. § 112, first paragraph for lack of enablement has been addressed and overcome. Reconsideration of the claims and withdrawal of the rejection thereof for lack of enablement under 35 U.S.C. §112, first paragraph is respectfully requested.

VII. Conclusion. This application is believed to be in condition for allowance, which is earnestly solicited. If the Examiner believes there are additional issues that may be addressed by an interview or a an Examiner's Amendment, the Examiner is invited to contact the undersigned attorney.

Dated: August 8, 2007

Respectfully submitted,

By 

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